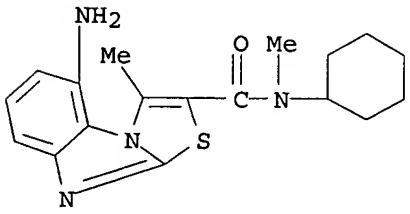
=> S 239801-59-3/RN

L5 1 239801-59-3/RN

=> D L5 SQIDE TOTAL

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **239801-59-3** REGISTRY
CN Thiazolo[3,2-a]benzimidazole-2-carboxamide, 5-amino-N-cyclohexyl-N,3-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)
MF C18 H22 N4 O S . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS



●2 HCl

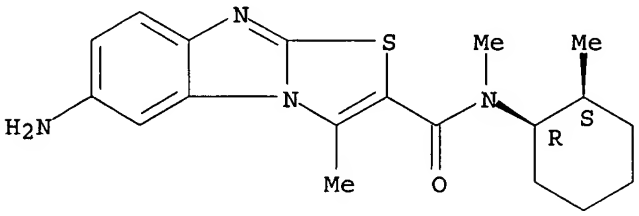
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

the compound in claim 6

394
397

L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **324022-11-9** REGISTRY
CN Thiazolo[3,2-a]benzimidazole-2-carboxamide, 6-amino-N,3-dimethyl-N-[(1R,2S)-2-methylcyclohexyl]-, dihydrochloride (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H24 N4 O S . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).

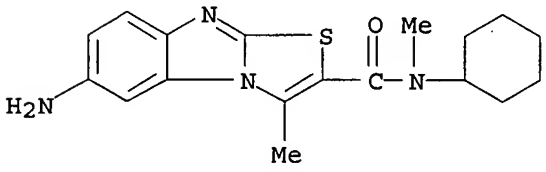


●2 HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

the instant compound in claim 6

L9 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **299901-50-1** REGISTRY
CN Thiazolo[3,2-a]benzimidazole-2-carboxamide, 6-amino-N-cyclohexyl-N,3-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)
MF C18 H22 N4 O S . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS



● 2 HCl

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L2 ANSWER 1 OF 5 EUROPATFULL COPYRIGHT 2002 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 1205187 EUROPATFULL EW 200220 FS OS
TITLE: REMEDIES FOR NEUROGENIC PAINS.
ARZNEI FUeR NEUROGENE SCHMERZEN.
REMEDES CONTRE LES DOULEURS NEUROGENES.
INVENTOR(S): Okada, Masamichi Yamanouchi Pharmaceutical Co.Ltd, 21, Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
Nagakura, Yukinori Yamanouchi Pharm. Co. Ltd, 21 Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
Kiso, Tetsuo Yamanouchi Pharmaceutical Co., Ltd., 21, Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
Toya, Takashi Yamanouchi Pharmaceutical Co., Ltd., 21, Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
Hayashibe, Satoshi Yamanouchi Pharm. Co.Ltd,, 21 Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP
PATENT ASSIGNEE(S): **YAMANOUCHI** PHARMACEUTICAL **CO**. **LTD**., No. 3-11 Nihonbashi-Honcho, 2-chome Chuo-ku, Tokyo 103-8411, JP
PATENT ASSIGNEE NO: 274784
AGENT: Geering, Keith Edwin et al., REDDIE & GROSE 16 Theobalds Road, London WC1X 8PL, GB
AGENT NUMBER: 30911
OTHER SOURCE: BEPA2002042 EP 1205187 A1 0013
SOURCE: Wila-EPZ-2002-H20-T1b
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Japanisch; Veroeffentlichung in Englisch; Verfahren in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO; R SI
PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG (Internationale Anmeldung)
PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 1205187	A1	20020515
'OFFENLEGUNGS' DATE:		20020515
APPLICATION INFO.: EP 2000-948290		20000801
PRIORITY APPLN. INFO.: JP 1999-218309		19990802
RELATED DOC. INFO.: WO 00-JP5074		000801 INTAKZ
WO 0108705		010208 INTPNR

L2 ANSWER 2 OF 5 EUROPATFULL COPYRIGHT 2002 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 1167369 EUROPATFULL EW 200201 FS OS
TITLE: NOVEL THIAZOLOBENZIMIDAZOLE DERIVATIVES.
NEUE THIAZOLOBENZIMIDAZOL-DERIVATE.
NOUVEAUX DERIVES DE THIAZOLOBENZIMIDAZOLE.
INVENTOR(S): HAYASHIBE, Satoshi, Yamanouchi Pharmac. Co., Ltd., 21, Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
ITAHANA, Hirotsune, Yamanouchi Pharmac. Co., Ltd., 21, Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
OKADA, Masamichi, Yamanouchi Pharmac. Co., Ltt., 21,

Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
KOHARA, Atsuyuki, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
MAENO, Kyoichi, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
YAHIRO, Kiyoshi, Yamanouchi Pharmac. Co., Ltd.,
21,Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
SHIMADA, Itsuro, Yamanouchi Pharmac. Co., Ltd.,
21,Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
TANABE, Kazuhito, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
NEGORO, Kenji, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
KAMIKUBO, Takashi, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP;
SAKAMOTO, Shuichi, Yamanouchi Pharmac. Co., Ltd., 21,
Miyukigaoka, Tsukuba-shi, Ibaraki 305-8585, JP

PATENT ASSIGNEE(S): **YAMANOUCHI** PHARMACEUTICAL **CO**.
LTD., No. 3-11 Nihonbashi-Honcho, 2-chome
Chuo-ku, Tokyo 103-8411, JP

PATENT ASSIGNEE NO: 274784

AGENT: Geering, Keith Edwin, REDDIE & GROSE 16 Theobalds Road,
London WC1X 8PL, GB

AGENT NUMBER: 30911

OTHER SOURCE: BEPA2002002 EP 1167369 A1 0040

SOURCE: Wila-EPZ-2002-H01-T1a

DOCUMENT TYPE: Patent

LANGUAGE: Anmeldung in Japanisch; Veroeffentlichung in Englisch;
Verfahren in Englisch

DESIGNATED STATES: R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R
GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R
SE; R AL; R LT; R LV; R MK; R RO; R SI

PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG (Internationale
Anmeldung)

PATENT INFORMATION:

	PATENT NO	KIND	DATE
	EP 1167369	A1	20020102
'OFFENLEGUNGS' DATE:			20020102
APPLICATION INFO.:	EP 2000-915350		20000405
PRIORITY APPLN. INFO.:	JP 1999-99062		19990406
RELATED DOC. INFO.:	WO 00-JP2199		000405 INTAKZ
	WO 0059913		001012 INTPNR

L2 ANSWER 3 OF 5 EUROPATFULL COPYRIGHT 2002 WILA

PATENT APPLICATION - PATENTANMELDUNG - DEMANDE DE BREVET

ACCESSION NUMBER: 1059090 EUROPATFULL EW 200050 FS OS

TITLE: REMEDIES FOR BRAIN INFARCTION.
MEDIKAMENTE GEGEN HIRNINFARKT.
MEDICAMENTS CONTRE L'INFARCISSEMENT DU CERVEAU.

INVENTOR(S): OKADA, M., Yamanouchi Pharmaceutical Co., Ltd., 21,
Miyukigaoka Tsukuba-shi, Ibaraki 305-8585, JP;
TAKAHASHI, M., Yamanouchi Pharmaceutical Co.,Ltd, 21,
Miyukigaoka Tsukuba-shi, Ibaraki 305-8585, JP;
HAYASHIBE, S., Yamanouchi Pharmaceutical Co.,Ltd., 21,
Miyukigaoka Tsukuba-shi, Ibaraki 305-8585, JP

PATENT ASSIGNEE(S): **YAMANOUCHI** PHARMACEUTICAL **CO**.
LTD., No. 3-11 Nihonbashi-Honcho, 2-chome

Chuo-ku, Tokyo 103-8411, JP
PATENT ASSIGNEE NO: 274784
AGENT: Geering, Keith Edwin, REDDIE & GROSE 16 Theobalds Road, London WC1X 8PL, GB
AGENT NUMBER: 30911
OTHER SOURCE: BEPA2000096 EP 1059090 A1 0011
SOURCE: Wila-EPZ-2000-H50-T1b
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Japanisch; Veroeffentlichung in Englisch; Verfahren in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R NL; R PT; R SE
PATENT INFO.PUB.TYPE: EPA1 EUROPAEISCHE PATENTANMELDUNG (Internationale Anmeldung)
PATENT INFORMATION:

PATENT NO	KIND	DATE
EP 1059090	A1	20001213
'OFFENLEGUNGS' DATE:		20001213
APPLICATION INFO.: EP 1999-906548		19990302
PRIORITY APPLN. INFO.: JP 1998-50241		19980303
RELATED DOC. INFO.: WO 99-JP995		990302 INTAKZ
WO 9944639		990910 INTPNR

L2 ANSWER 4 OF 5 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2001-182868 [18] WPIDS
DOC. NO. CPI: C2001-054575
TITLE: Remedies with reduced side-effects for neurogenic pains e.g. due to diabetes and nervous tension comprises systemic administration of an **mGluR1** receptor antagonist, conveniently operable by patients.
DERWENT CLASS: B04
INVENTOR(S): HAYASHIBE, S; KISO, T; NAGAKURA, Y; OKADA, M; TOYA, T
PATENT ASSIGNEE(S): (YAMA) **YAMANOUCHI PHARM CO LTD**
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001008705	A1	20010208	(200118)*	JA	21
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000061820	A	20010219	(200129)		
EP 1205187	A1	20020515	(200239)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001008705	A1	WO 2000-JP5074	20000801
AU 2000061820	A	AU 2000-61820	20000801
EP 1205187	A1	EP 2000-948290	20000801
		WO 2000-JP5074	20000801

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000061820	A	Based on	WO 200108705
EP 1205187	A1	Based on	WO 200108705

PRIORITY APPLN. INFO: JP 1999-218309 19990802

L2 ANSWER 5 OF 5 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-540747 [45] WPIDS
DOC. NO. CPI: C1999-157977
TITLE: Agent for treating brain infarction comprising **mGluR1** antagonist, preferably thiazolo-benzimidazole derivative.
DERWENT CLASS: B02
INVENTOR(S): HAYASHIBE, S; OKADA, M; TAKAHASHI, M
PATENT ASSIGNEE(S): (YAMA) **YAMANOUCHI PHARM CO LTD**
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9944639	A1	19990910	(199945)*	JA	19
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AU AZ BA BB BG BR BY CA CN CU CZ EE GE GH GM HR HU ID IL IN IS JP KE KG KR KZ LC LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9926426	A	19990920	(200007)		
EP 1059090	A1	20001213	(200066)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9944639	A1	WO 1999-JP995	19990302
AU 9926426	A	AU 1999-26426	19990302
EP 1059090	A1	EP 1999-906548	19990302
		WO 1999-JP995	19990302

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9926426	A	Based on	WO 9944639
EP 1059090	A1	Based on	WO 9944639

PRIORITY APPLN. INFO: JP 1998-50241 19980303

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:725639 CAPLUS
DOCUMENT NUMBER: 133:281784
TITLE: Preparation of thiazolobenzimidazole derivatives as drugs with affinity for metabotropic glutamate receptors
INVENTOR(S): Hayashibe, Satoshi; Itahana, Hirotsune; Okada, Masamichi; Kohara, Atsuyuki; Maeno, Kyoichi; Yahiro, Kiyoshi; Shimada, Itsuro; Tanabe, Kazuhito; Negoro, Kenji; Kamikubo, Takashi; Sakamoto, Shuichi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan; et al.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059913	A1	20001012	WO 2000-JP2199	20000405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CN 1271731	A	20001101	CN 2000-104936	20000331
JP 2000351782	A2	20001219	JP 2000-102893	20000405
EP 1167369	A1	20020102	EP 2000-915350	20000405
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1999-99062 A 19990406
WO 2000-JP2199 W 20000405
OTHER SOURCE(S): MARPAT 133:281784

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             1 239801-59-3
             0 239801-59-3D
L1           1 239801-59-3/RN
                 (239801-59-3 (NOTL) 239801-59-3D )

=> d ibib

L1   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         1999:576811  CAPLUS
DOCUMENT NUMBER:          131:179814
TITLE:                    Remedies for brain infarction
INVENTOR(S):              Okada, Masamichi; Takahashi, Masayasu; Hayashibe,
                          Satoshi
PATENT ASSIGNEE(S):       Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE:                   PCT Int. Appl., 19 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
     ---------------   ----  --------       ---------------   --------
     WO 9944639         A1   19990910       WO 1999-JP995     19990302
         W:  AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
             LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI,
             SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
             ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9926426         A1   19990920       AU 1999-26426     19990302
     EP 1059090         A1   20001213       EP 1999-906548    19990302
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
FI
PRIORITY APPLN. INFO.:                      JP 1998-50241     A  19980303
                                            WO 1999-JP995     W  19990302
REFERENCE COUNT:          4      THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT
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             1 324022-11-9
             0 324022-11-9D
L3           1 324022-11-9/RN
                 (324022-11-9 (NOTL) 324022-11-9D )

=> d ibib

L3   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2001:100999  CAPLUS
DOCUMENT NUMBER:          134:141763
TITLE:                    Remedies for neurogenic pains
INVENTOR(S):              Okada, Masamichi; Nagakura, Yukinori; Kiso, Tetsuo;
                          Toya, Takashi; Hayashibe, Satoshi
PATENT ASSIGNEE(S):       Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE:                   PCT Int. Appl., 21 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2001008705      A1   20010208       WO 2000-JP5074   20000801
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1205187         A1   20020515       EP 2000-948290   20000801
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.:                    JP 1999-218309   A  19990802
                                          WO 2000-JP5074   W  20000801
REFERENCE COUNT:          6      THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT
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=> d ibib 1-2

L2 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:100999 CAPLUS
DOCUMENT NUMBER: 134:141763
TITLE: Remedies for neurogenic pains
INVENTOR(S): Okada, Masamichi; Nagakura, Yukinori; Kiso, Tetsuo; Toya, Takashi; Hayashibe, Satoshi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

this PCT of the application herein

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008705	A1	20010208	WO 2000-JP5074	20000801
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1205187	A1	20020515	EP 2000-948290	20000801
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: JP 1999-218309 A 19990802
WO 2000-JP5074 W 20000801
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:725639 CAPLUS
DOCUMENT NUMBER: 133:281784
TITLE: Preparation of thiazolobenzimidazole derivatives as drugs with affinity for metabotropic glutamate receptors
INVENTOR(S): Hayashibe, Satoshi; Itahana, Hirotsune; Okada, Masamichi; Kohara, Atsuyuki; Maeno, Kyoichi; Yahiro, Kiyoshi; Shimada, Itsuro; Tanabe, Kazuhito; Negoro, Kenji; Kamikubo, Takashi; Sakamoto, Shuichi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan; et al.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059913	A1	20001012	WO 2000-JP2199	20000405
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,				

CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CN 1271731	A	20001101	CN 2000-104936	20000331
JP 2000351782	A2	20001219	JP 2000-102893	20000405
EP 1167369	A1	20020102	EP 2000-915350	20000405

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:	JP 1999-99062	A	19990406
	WO 2000-JP2199	W	20000405

OTHER SOURCE(S): MARPAT 133:281784

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=> d his

     (FILE 'HOME' ENTERED AT 14:15:16 ON 11 MAR 2003)

     FILE 'CAPLUS' ENTERED AT 14:15:23 ON 11 MAR 2003
L1             1 S 239801-59-3/RN
L2             2 S 299901-50-1/RN
L3             1 S 324022-11-9/RN
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Glutamate receptor antagonists for neuropathic pain

12-13 17-22
exact bonds :
1-2 1-5 1-10 2-3 4-5 5-11 8-24 10-12 11-12 13-14 13-15 15-16 15-23
16-17 16-21 17-18 18-19 19-20 20-21
normalized bonds :
3-4 3-6 4-9 6-7 7-8 8-9

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom
19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS

Stereo Bonds:

16-15 (Single Hash).
22-17 (Single Hash).

Stereo Chiral Centers:

16   (Parity=Even)
17   (Parity=Odd)

Stereo RSS Sets:

Type=Relative (Default). 2 Nodes= 16 17

L3   STRUCTURE UPLOADED

=> s L3
SAMPLE SEARCH INITIATED 08:38:12 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   14 TO ITERATE

100.0% PROCESSED   14 ITERATIONS   0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 56 TO   504
PROJECTED ANSWERS: 0 TO   0

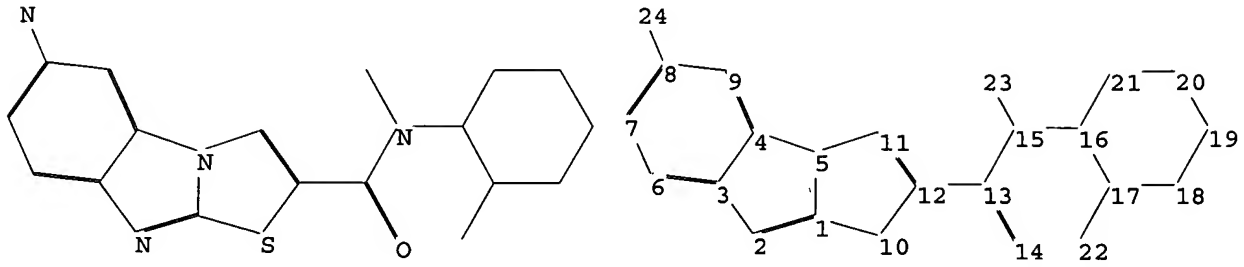
L4   0 SEA SSS SAM L3

=> d L2 rn

L2   ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN   299900-32-6 REGISTRY

=>
Uploading C:\Program Files\Stnexp\Queries\10031401bracem.str

Glutamate receptor antagonists for neuropathic pain



ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 16 17 18 19 20 21
ring/chain nodes :
13 14 15 22 23 24
chain bonds :
15-16 17-22
ring/chain bonds :
8-24 12-13 13-14 13-15 15-23
ring bonds :
1-2 1-5 1-10 2-3 3-4 3-6 4-5 4-9 5-11 6-7 7-8 8-9 10-12 11-12 16-17
16-21 17-18 18-19 19-20 20-21
exact/norm bonds :
12-13 15-16
exact bonds :
1-2 1-5 1-10 2-3 4-5 5-11 8-24 10-12 11-12 13-14 13-15 15-23 16-17
16-21 17-18 17-22 18-19 19-20 20-21
normalized bonds :
3-4 3-6 4-9 6-7 7-8 8-9

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:Atom
19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS

L5 STRUCTURE UPLOADED

=> s l5
SAMPLE SEARCH INITIATED 08:40:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 5 TO ITERATE

100.0% PROCESSED 5 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 5 TO 234
PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

=> file home

Glutamate receptor antagonists for neuropathic pain

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS 4	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS 5	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS 6	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS 7	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS 8	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS 9	JAN 30	Saved answer limit increased
NEWS 10	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS 11	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS 12	FEB 22	Status of current WO (PCT) information on STN
NEWS 13	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS 14	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS 15	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS 16	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS 17	FEB 28	TOXCENTER reloaded with enhancements
NEWS 18	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS 19	MAR 01	INSPEC reloaded and enhanced
NEWS 20	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes
NEWS 21	MAR 08	X.25 communication option no longer available after June 2006

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

Glutamate receptor antagonists for neuropathic pain

FILE 'HOME' ENTERED AT 08:35:12 ON 21 MAR 2006

=> file registry
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 08:35:24 ON 21 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8
DICTIONARY FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************
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Structure search iteration limits have been increased. See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
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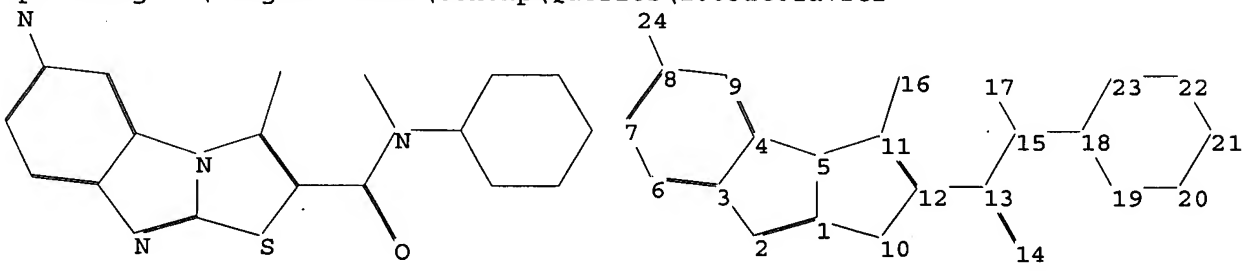

Glutamate receptor antagonists for neuropathic pain

```
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  18  19  20  21  22  23
ring/chain nodes :
13  14  15  16  17  24
ring/chain bonds :
8-24  11-16  12-13  13-14  13-15  15-17  15-18
ring bonds :
1-2  1-5  1-10  2-3  3-4  3-6  4-5  4-9  5-11  6-7  7-8  8-9  10-12  11-12  18-19
18-23  19-20  20-21  21-22  22-23
exact/norm bonds :
11-16  12-13
exact bonds :
1-2  1-5  1-10  2-3  4-5  5-11  8-24  10-12  11-12  13-14  13-15  15-17  15-18
18-19  18-23  19-20  20-21  21-22  22-23
normalized bonds :
3-4  3-6  4-9  6-7  7-8  8-9


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS  18:Atom
19:Atom  20:Atom  21:Atom  22:Atom  23:Atom  24:CLASS



L1      STRUCTURE UPLOADED

=> s L1
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SAMPLE SCREEN SEARCH COMPLETED -       14 TO ITERATE

100.0% PROCESSED       14 ITERATIONS                                 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:           56 TO      504
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> d 1 full
'FULL' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG     - RN
SAM     - Index Name, MF, and structure - no RN
FIDE    - All substance data, except sequence data
IDE     - FIDE, but only 50 names
SQIDE   - IDE, plus sequence data
SQIDE3  - Same as SQIDE, but 3-letter amino acid codes are used
SQD     - Protein sequence data, includes RN
SQD3    - Same as SQD, but 3-letter amino acid codes are used
SQN     - Protein sequence name information, includes RN

CALC    - Table of calculated properties
```

Glutamate receptor antagonists for neuropathic pain

EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

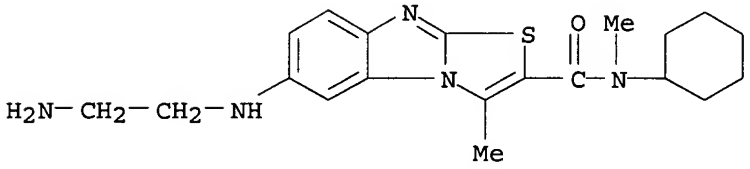
HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):all

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN 299900-32-6 REGISTRY
ED Entered STN: 27 Oct 2000
CN Thiazolo[3,2-a]benzimidazole-2-carboxamide, 6-[(2-aminoethyl)amino]-N-cyclohexyl-N,3-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)
MF C20 H27 N5 O S . Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (764636-79-5)

Ring System Data

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C6	C6	6	C6	46.150.1	1
C3NS-C3N2-C6	NCSC2-NCNC2-C6	5-5-6	C9N2S	1341.223.4	1

Glutamate receptor antagonists for neuropathic pain



● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

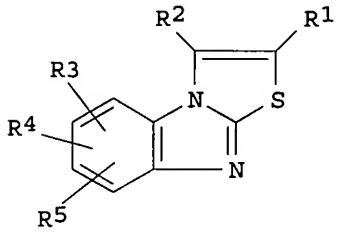
REFERENCE 1

AN 133:281784 CA
TI Preparation of thiazolobenzimidazole derivatives as drugs with affinity for metabotropic glutamate receptors
IN Hayashibe, Satoshi; Itahana, Hirotsune; Okada, Masamichi; Kohara, Atsuyuki; Maeno, Kyoichi; Yahiro, Kiyoshi; Shimada, Itsuro; Tanabe, Kazuhito; Negoro, Kenji; Kamikubo, Takashi; Sakamoto, Shuichi
PA Yamanouchi Pharmaceutical Co., Ltd., Japan; et al.
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07D513-04
ICS A61K031-429; A61K031-5383; A61K031-454; A61K031-4439; A61K031-435; A61P043-00; A61P025-28; A61P009-10
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059913	A1	20001012	WO 2000-JP2199	20000405
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CN 1271731	A	20001101	CN 2000-104936	20000331
	CN 1120842	B	20030910		
	CA 2365419	AA	20001012	CA 2000-2365419	20000405
	JP 2000351782	A2	20001219	JP 2000-102893	20000405
	EP 1167369	A1	20020102	EP 2000-915350	20000405
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6642264	B1	20031104	US 2001-958174	20011005
PRAI	JP 1999-99062	19990406			
	WO 2000-JP2199	20000405			

GI

Glutamate receptor antagonists for neuropathic pain



I

AB The title compds. I [R1 is optionally substituted carbamoyl, carbonyl, oxy, amino, carbonylamino, or the like; R2 is hydrogen, lower alkyl, or the like; and R3 , R4 and R5 are each independently hydrogen, lower alkyl, or the like] are prepared In an in vitro assay for affinity for the title receptors, N-cyclohexyl-6-glycylamino-N-methylthiazolo[3,2-a]benzimidazole-2-carboxamide showed IC50 of 20 nM.

ST thiazolobenzimidazole prepn metabotropic glutamate receptor affinity; metabotropic glutamate receptor affinity thiazolobenzimidazole prepn

IT Brain, disease
(infarction; preparation and effect of thiazolobenzimidazole derivs.)

IT Glutamate antagonists
(mGluR1; thiazolobenzimidazole derivs.)

IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabotropic, mGluR1; preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

IT 299899-98-2P 299900-55-3P 299900-68-8P 299900-80-4P 299900-86-0P
299900-87-1P 299900-90-6P 299900-92-8P 299900-93-9P 299900-94-0P
299901-59-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

IT 299899-96-0P 299899-97-1P 299899-99-3P 299900-00-8P 299900-01-9P
299900-02-0P 299900-03-1P 299900-04-2P 299900-06-4P 299900-07-5P
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299900-18-8P 299900-19-9P 299900-20-2P 299900-21-3P 299900-22-4P
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299900-28-0P 299900-29-1P 299900-30-4P 299900-31-5P 299900-32-6P
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299900-78-0P 299900-79-1P 299900-81-5P 299900-82-6P 299900-83-7P
299900-84-8P 299900-85-9P 299900-88-2P 299900-89-3P 299900-91-7P
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299901-30-7P 299901-31-8P

Glutamate receptor antagonists for neuropathic pain

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

IT 50-00-0, Formaldehyde, reactions 78-95-5, Chloroacetone 100-60-7, N-Methylcyclohexylamine 109-85-3, 2-Methoxyethylamine 109-89-7, Diethylamine, reactions 539-88-8, Ethyl levulinate 583-39-1, 2-Mercaptobenzimidazole 609-15-4, Ethyl 2-chloroacetoacetate 822-87-7, 2-Chlorocyclohexanone 2719-27-9, Cyclohexanecarbonyl chloride 4009-98-7, (Methoxymethyl)triphenylphosphonium chloride 4530-20-5, N-(tert-Butoxycarbonyl)glycine 5268-71-3 5268-72-4 26153-91-3, N-Methylneopentylamine 50630-93-8, Methyl-t3 iodide 51579-10-3 58089-25-1, 2-Mercaptobenzimidazole-5-carboxylic acid 58479-61-1, tert-Butyldiphenylsilyl chloride 92807-01-7 101226-33-9 299901-57-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

IT 5268-73-5P, 3-Methylthiazolo[3,2-a]benzimidazole 5268-74-6P 16458-82-5P 299901-32-9P 299901-33-0P 299901-34-1P 299901-35-2P 299901-36-3P 299901-37-4P 299901-38-5P 299901-39-6P 299901-41-0P 299901-42-1P 299901-43-2P 299901-44-3P 299901-45-4P 299901-46-5P 299901-47-6P 299901-48-7P 299901-49-8P 299901-50-1P 299901-51-2P 299901-52-3P 299901-53-4P 299901-54-5P 299901-55-6P 299901-56-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

IT 299901-58-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of thiazolobenzimidazole derivs. as drugs with affinity for metabotropic glutamate receptors)

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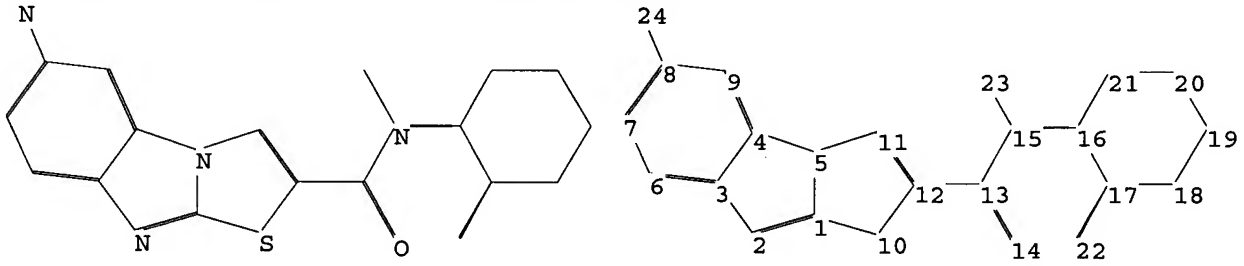

ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 16 17 18 19 20 21
ring/chain nodes :
13 14 15 22 23 24
ring/chain bonds :
8-24 12-13 13-14 13-15 15-16 15-23 17-22
ring bonds :
1-2 1-5 1-10 2-3 3-4 3-6 4-5 4-9 5-11 6-7 7-8 8-9 10-12 11-12 16-17 16-21 17-18 18-19 19-20 20-21
exact/norm bonds :

Glutamate receptor antagonists for neuropathic pain

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	9.83	10.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.71	-0.71

FILE 'HOME' ENTERED AT 08:41:06 ON 21 MAR 2006

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.26	11.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.71

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FILE COVERS 1907 - 21 Mar 2006 VOL 144 ISS 13
FILE LAST UPDATED: 20 Mar 2006 (20060320/ED)

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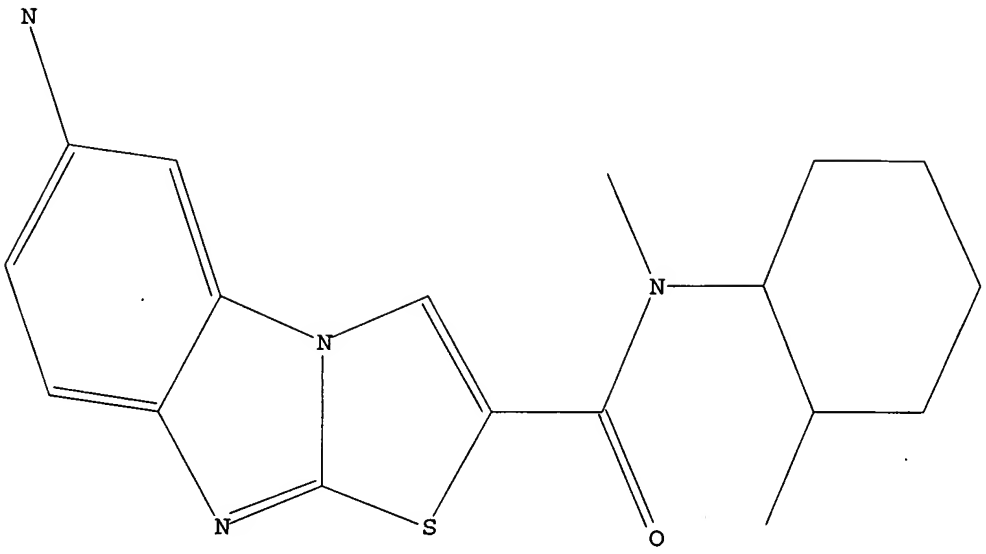
=> d l6
L6 HAS NO ANSWERS
L5 STR

Glutamate receptor antagonists for neuropathic pain



Structure attributes must be viewed using STN Express query preparation.
L6 0 SEA FILE=REGISTRY SSS SAM L5

=> s L2 and neuropath?
1 L2
19414 NEUROPATH?
L7 0 L2 AND NEUROPATH?

=> s L2 and pain
1 L2
42790 PAIN
L8 0 L2 AND PAIN

=> s l2
L9 1 L2

=> d l2 full
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n

=> file pharmacology
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	5.74	17.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.71

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Glutamate receptor antagonists for neuropathic pain

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FILE 'IFIPAT' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'IMSDRUGNEWS' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'IMSPATENTS' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'IMSPRODUCT' ENTERED AT 08:47:23 ON 21 MAR 2006

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FILE 'KOSMET' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'LIFESCI' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'MEDLINE' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'NAPRALERT' ENTERED AT 08:47:23 ON 21 MAR 2006

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FILE 'PCTFULL' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PHAR' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PHARMAML' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PHIC' ENTERED AT 08:47:23 ON 21 MAR 2006

Glutamate receptor antagonists for neuropathic pain

FILE 'PHIN' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PROMT' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PROUSDDR' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'PS' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'RDISCLOSURE' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'SCISEARCH' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'SYNTHLINE' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'TOXCENTER' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'USAN' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'USPATFULL' ENTERED AT 08:47:23 ON 21 MAR 2006

FILE 'USPAT2' ENTERED AT 08:47:23 ON 21 MAR 2006

=> index L1
'L1' IS NOT A VALID FILE NAME
ENTER A FILE NAME OR (IGNORE):
ENTER A FILE NAME OR (IGNORE):
ENTER A FILE NAME OR (IGNORE):ignore
AT LEAST TWO FILES ARE NEEDED FOR STNINDEX
SESSION CONTINUES IN THE PREVIOUS FILE ENVIRONMENT
To see a list of files and clusters that may be used in the INDEX command, enter HELP FILE NAMES or HELP CLUSTER NAMES at an arrow prompt. Only the learning files and NBSFLUIDS may not be used in STNINDEX.

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	74.51	91.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.71

FILE 'CAPLUS' ENTERED AT 08:48:17 ON 21 MAR 2006

Glutamate receptor antagonists for neuropathic pain

FILE COVERS 1907 - 21 Mar 2006 VOL 144 ISS 13
FILE LAST UPDATED: 20 Mar 2006 (20060320/ED)

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=> s L1 and neuropath?
REGIstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 08:48:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 14 TO ITERATE

100.0% PROCESSED 14 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 56 TO 504
PROJECTED ANSWERS: 1 TO 80

L10 1 SEA SSS SAM L1

L11 1 L10

19414 NEUROPATH?
L12 0 L11 AND NEUROPATH?

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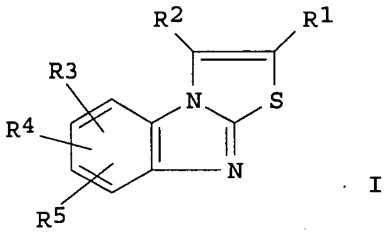
1 299900-32-6
0 299900-32-6D
L13 1 299900-32-6/RN
(299900-32-6 (NOTL) 299900-32-6D)

=> d L13 tot abs

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
GI

Glutamate receptor antagonists for neuropathic pain



I

AB The title compds. I [R1 is optionally substituted carbamoyl, carbonyl, oxy, amino, carbonylamino, or the like; R2 is hydrogen, lower alkyl, or the like; and R3 , R4 and R5 are each independently hydrogen, lower alkyl, or the like] are prepared In an in vitro assay for affinity for the title receptors, N-cyclohexyl-6-glycylamino-N-methylthiazolo[3,2-a]benzimidazole-2-carboxamide showed IC50 of 20 nM.

=> file pharmacology
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	8.83	101.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-1.46

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Glutamate receptor antagonists for neuropathic pain

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Glutamate receptor antagonists for neuropathic pain

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L14          2 299900-32-6/RN

=> d tot ti

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
TI   Preparation of thiazolobenzimidazole derivatives as drugs with affinity
```

Glutamate receptor antagonists for neuropathic pain

for metabotropic glutamate receptors

L14 ANSWER 2 OF 2 USPATFULL on STN
TI Thiazolobenzoimidazole derivatives

=> d tot abs

L14 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
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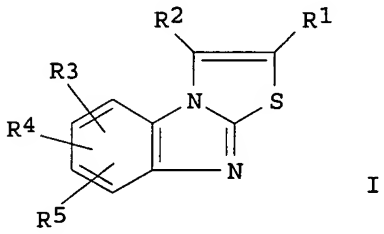

I

AB The title compds. I [R1 is optionally substituted carbamoyl, carbonyl, oxy, amino, carbonylamino, or the like; R2 is hydrogen, lower alkyl, or the like; and R3 , R4 and R5 are each independently hydrogen, lower alkyl, or the like] are prepared In an in vitro assay for affinity for the title receptors, N-cyclohexyl-6-glycylamino-N-methylthiazolo[3,2-a]benzimidazole-2-carboxamide showed IC50 of 20 nM.

L14 ANSWER 2 OF 2 USPATFULL on STN
AB This invention relates to novel thiazolo[3,2-a]benzoimidazole derivatives represented by the following general formula (I). The compounds provided by the invention act specifically on metabotropic glutamate receptors and are used as medicaments. The invention also provides novel compounds useful as intermediates for the synthesis of the compounds of the invention. ##STR1##

(Symbols in the formula represent the following meanings. R.sup.1: carbamoyl, carbonyl, oxy, amino, carbonylamino or the like which may be substituted; R.sup.2: hydrogen, lower alkyl or the like; and R.sup.3, R.sup.4 and R.sup.5: hydrogen, lower alkyl and the like which may be the same or different from one another.)

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l14 2 pn

L14 ANSWER 2 OF 2 USPATFULL on STN
PI US 6642264 B1 20031104
WO 2000059913 20001012

=> file medline

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FULL ESTIMATED COST	82.34	183.62

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

Glutamate receptor antagonists for neuropathic pain

CA SUBSCRIBER PRICE -0.75 -2.21

FILE 'MEDLINE' ENTERED AT 08:52:27 ON 21 MAR 2006

FILE LAST UPDATED: 18 MAR 2006 (20060318/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s mGluR1
L15         596 MGLUR1

=> s L15 and antagon?
         541277 ANTAGON?
L16         296 L15 AND ANTAGON?

=> s L16 and neuropath?
          57825 NEUROPATH?
L17           4 L16 AND NEUROPATH?

=> d 1-4 ti

L17  ANSWER 1 OF 4      MEDLINE on STN
TI   Role of central and peripheral mGluR5 receptors in post-operative pain in
     rats.

L17  ANSWER 2 OF 4      MEDLINE on STN
TI   Neuroprotective activity of metabotropic glutamate receptor ligands.

L17  ANSWER 3 OF 4      MEDLINE on STN
TI   Differential effects of NMDA and group I mGluR antagonists on
     both nociception and spinal cord protein kinase C translocation in the
     formalin test and a model of neuropathic pain in rats.

L17  ANSWER 4 OF 4      MEDLINE on STN
TI   In vivo antinociceptive activity of anti-rat mGluR1 and mGluR5
     antibodies in rats.


=> d L17 2 abs

L17  ANSWER 2 OF 4      MEDLINE on STN
AB   Metabotropic glutamate receptors form a family of currently eight subtypes
     (mGluR1-8), subdivided into three groups (I-III). Activation of
     group-II (mGluR2 and -3) or group-III metabotropic glutamate receptors
     (mGluR4, -6, -7 and -8) has been established to be neuroprotective in
     vitro and in vivo. In contrast, group-I mGluRs (mGluR1 and -5)
```

need to be **antagonized** in order to evoke protection. Initially, all neuroprotective mGluR ligands were analogues of L-glutamate. Those compounds were valuable to demonstrate protection in vitro, but showed limited applicability in animal models, particularly in chronic tests, due to low blood-brain-barrier penetration. Recently, systemically active and more potent and selective ligands became available, e.g., the group-II mGluR agonists LY354740 and LY379268 or group-I **antagonists** like MPEP (mGluR5-selective) and BAY36-7620 (**mGluR1**-selective). This new generation of pharmacological agents allows a more stringent assessment of the role of individual mGluR-subtypes or groups of receptors in various nervous system disorders, including ischaemia-induced brain damage, traumatic brain injury, Huntington's and Parkinson's-like pathology or epilepsy. Moreover, the use of genetically modified animals (e.g., knock-out mice) is starting to shed light on specific functions of mGluR-subtypes in experimental **neuropathologies.**

=> d L17 3 abs

L17 ANSWER 3 OF 4 MEDLINE on STN

AB Coincident with nociception, both noxious chemical stimulation of the hind paw and chronic constriction injury (CCI) of the sciatic nerve produce an increase in protein kinase C (PKC) translocation in the spinal cord of rats. Noxious stimulus-induced PKC translocation likely depends on glutamate activity at either N-methyl-D-aspartate (NMDA) receptors or group I metabotropic glutamate receptors (**mGluR1**/5) in the spinal cord dorsal horn. This study compares nociceptive responses to, and the alterations in membrane-associated PKC, induced by noxious chemical stimulation of the hindpaw and CCI of the sciatic nerve, as well as their modulation by both NMDA and **mGluR1**/5 receptor **antagonists.** Three groups of rats were given a single intrathecal (i.t.) injection of either vehicle, dizocilpine maleate (MK-801, 60 nmol), an NMDA receptor **antagonist**, or (S)-4-carboxyphenylglycine (S)-4CPG, (150 nmol), an **mGluR1**/5 **antagonist**, 10 min prior to a 50 microl of 2.5% formalin injection into the ventral surface of one hind paw. Another three groups of rats were given twice daily injections of either vehicle, MK-801 (30 nmol) or (S)-4CPG (90 nmol) i.t. for 5 days starting 30 min before CCI or sham injury of the sciatic nerve. Nociceptive responses were assessed for a 60 min period after the formalin injection in the first three groups, and tests of mechanical and cold allodynia were performed on days 4, 8, 12 and 16 after CCI for the latter three groups. Furthermore, changes in the levels of membrane-associated PKC, as assayed by quantitative autoradiography of the specific binding of [3H]-phorbol 12,13-dibutyrate ([3H]-PDBu) in the dorsal horn of the lumbar spinal cord sections, were assessed in formalin-injected rats (at 5, 25 and 60 min) and in **neuropathic** rats 5 days after CCI, treated (as above) with vehicle, MK-801 or (S)-4CPG. The results indicate that i.t. treatment with MK-801 significantly reduced nociceptive scores in the formalin test and also produced a significant suppression of formalin-induced increases in [3H]-PDBu binding in laminae I-II, III-VI and X of the lumbar spinal cord. In contrast, i.t. treatment with (S)-4CPG failed to significantly affect either nociceptive behaviours in the formalin test or formalin-induced increases in [3H]-PDBu binding in laminae I-II and III-VI of the lumbar spinal cord. On the other hand, i.t. treatment with either MK-801 or (S)-4CPG produced a significant reduction in mechanical and cold hypersensitivity, as well as [3H]-PDBu binding in laminae I-II and III-VI of the lumbar spinal cord, after CCI. These results suggest that while NMDA, but not **mGluR1**/5, receptors are involved in translocation of PKC and nociception in a model of persistent acute pain, both types of receptors influence the translocation of PKC in dorsal horn and mechanical and cold allodynia in a model of chronic **neuropathic** pain.

Glutamate receptor antagonists for neuropathic pain

```
=> d L17 3 full
'FULL' IS NOT A VALID FORMAT FOR FILE 'MEDLINE'

The following are valid formats:

The default display format is BIB.

ABS ---- AB
ALL ---- AN, DN, TI, AU, CS, NC, SO, CM, CY, DT, LA, FS, OS, EM,
         ED, AB, ST, CT, NA, RN, CN, GEN
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CBIB --- AN, DN, TI, AU, CS, NC, SO, CY, DT, LA, FS, OS, EM, ED
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IBIB --- BIB, indented with text labels
IND ---- ST, CT, NA, RN, CN, GEN
SAM ---- TI, ST, CT, NA, RN, CN, GEN
TRI ---- TI, ST, CT, NA, RN, CN, GEN
TRIAL -- TI, ST, CT, NA, RN, CN, GEN
HIT ---- All fields containing hit terms
HITIND - IND
KWIC --- All hit terms plus 20 words on either side
OCC ---- List of display fields containing hit terms

Hit terms will be highlighted in all available fields except CM and
PY.

To display a particular field or fields,  enter the display field
codes.  For a list of display field codes, enter 'HELP DFIELDS'
at an arrow prompt (=>).  Examples of formats include: 'BIB';
'AB'; 'SO,ST'.  You may specify the format fields in any order,
and the information will be displayed in the same order as the
format specification.

The same formats (except for HIT, HITIND, KWIC, and OCC) may be
used with the DISPLAY ACC command to display the record for a
specified Accession Number.
ENTER DISPLAY FORMAT (BIB):bib

L17  ANSWER 3 OF 4     MEDLINE on STN
AN   2001530686     MEDLINE
DN   PubMed ID: 11576741
TI   Differential effects of NMDA and group I mGluR antagonists on
     both nociception and spinal cord protein kinase C translocation in the
     formalin test and a model of neuropathic pain in rats.
AU   Yashpal K; Fisher K; Chabot J G; Coderre T J
CS   Pain Mechanisms Laboratory, Clinical Research Institute of Montreal,
     McGill University, Montreal, Quebec, Canada H3G 1Y6.
SO   Pain, (2001 Oct) Vol. 94, No. 1, pp. 17-29.
     Journal code: 7508686. ISSN: 0304-3959.
CY   Netherlands
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200112
ED   Entered STN: 20011001
     Last Updated on STN: 20020122
     Entered Medline: 20011207


=> s L16 and pain
```

Glutamate receptor antagonists for neuropathic pain

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        264488 PAIN
L18         28 L16 AND PAIN

=> s L18 and py<2001
      12889601 PY<2001
                  (PY<20010000)
L19          8 L18 AND PY<2001

=> d 1-8 ti

L19  ANSWER 1 OF 8      MEDLINE on STN
TI   Methylphenylethynylpyridine (MPEP) Novartis.

L19  ANSWER 2 OF 8      MEDLINE on STN
TI   Group I metabotropic glutamate receptors: implications for brain diseases.

L19  ANSWER 3 OF 8      MEDLINE on STN
TI   Role of metabotropic glutamate receptor subtype mGluR1 in brief
     nociception and central sensitization of primate STT cells.

L19  ANSWER 4 OF 8      MEDLINE on STN
TI   Hyperalgesia and allodynia induced by intrathecal (RS)-
     dihydroxyphenylglycine in rats.

L19  ANSWER 5 OF 8      MEDLINE on STN
TI   In vivo antinociceptive activity of anti-rat mGluR1 and mGluR5
     antibodies in rats.

L19  ANSWER 6 OF 8      MEDLINE on STN
TI   Behavioural and electrophysiological evidence supporting a role for group
     I metabotropic glutamate receptors in the mediation of nociceptive inputs
     to the rat spinal cord.

L19  ANSWER 7 OF 8      MEDLINE on STN
TI   Pharmacological characterization of 1-aminoindan-1,5-dicarboxylic acid, a
     potent mGluR1 antagonist.

L19  ANSWER 8 OF 8      MEDLINE on STN
TI   The contribution of metabotropic glutamate receptors (mGluRs) to
     formalin-induced nociception.


=> d 1-8 abs

L19  ANSWER 1 OF 8      MEDLINE on STN
AB   SIBIA and Novartis are investigating the use of excitatory amino acid
     agonists and antagonists for the metabotropic receptor and the
     ionotropic receptors AMPA and NMDA.  Preliminary experiments indicate they
     may have potential in the treatment of epilepsy, stroke, anxiety,
     pain and neurodegenerative disease.  Methylphenylethynylpyridine
     (MPEP) is the lead compound in the series [347212].  Other compounds in
     the series that arose from the collaboration were SIB-1893, and its
     equipotent analog, SIB-1757, both of which are subtype-selective, potent
     antagonists of mGluR5.  Chemical derivation of SIB-1893 resulted
     in the discovery of MPEP, a selective, systemically active noncompetitive
     mGluR5 antagonist.  Studies using these agents have yielded data
     to support the involvement of mGluR5 in inflammatory mechanical
     hyperalgesia [311829], [311828], [311823], [311880], [319655].  MPEP is
     the most potent of these compounds with an IC50 value of 12 nM for
     inhibition of quisqualate-stimulated phosphoinositide hydrolysis in
     recombinant human mGluR5a-expressing cells.  MPEP exhibited no cross
     reactivity with mGluR1 and other mGluRs, or against
     representative NMDA, AMPA and kainate receptors up to concentrations of
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100 microM. The compound, administered orally (100 mg/kg) produced a 70% reversal of mechanical hyperalgesia in the Freund's complete adjuvant model of inflammatory **pain** [319261]. By October 1999, investigations with SIB-1757 and SIB-1893 had been discontinued in favor of MPEP [347212].

L19 ANSWER 2 OF 8 MEDLINE on STN

AB Glutamate is the major excitatory neurotransmitter in the brain and plays a unique role in a variety of central nervous system (CNS) functions. The discovery of the metabotropic receptors (mGluRs), a family of G-protein coupled receptors than can be activated by glutamate, has led to an impressive number of studies in recent years aimed at understanding their biochemical, physiological and pharmacological characteristics. The eight mGluRs now known are divided into three groups according to their sequence homology, signal transduction mechanisms, and agonist selectivity. Group I mGluRs include **mGluR1** and mGluR5, which are linked to the activation of phospholipase C; Groups II and III include all others and are negatively coupled to adenylyl cyclases. The availability in recent years of agents selective for Group I mGluRs has made possible the study of the physiological roles of these receptors in the CNS. In addition to mediating glutamatergic neurotransmission, Group I mGluRs can modulate other neurotransmitter receptors, including GABA and the ionotropic glutamate receptors. Group I mGluRs are involved in many CNS functions and may participate in a variety of disorders such as **pain**, epilepsy, ischemia, and chronic neurodegenerative diseases. This class of receptor may provide important pharmacological therapeutic targets and elucidating its functions will be relevant to develop new treatments for neurological and psychiatric disorders in which glutamatergic neurotransmission is abnormally regulated. In this review anatomical, physiological and pharmacological results are presented with a special emphasis on the role of Group I mGluRs in functional and pathological processes.

L19 ANSWER 3 OF 8 MEDLINE on STN

AB G-protein coupled metabotropic glutamate receptors (mGluRs) are important modulators of synaptic transmission in the mammalian CNS and have been implicated in various forms of neuroplasticity and nervous system disorders. Increasing evidence also suggests an involvement of mGluRs in nociception and **pain** behavior although the contribution of individual mGluR subtypes is not yet clear. Subtypes **mGluR1** and mGluR5 are classified as group I mGluRs and share the ability to stimulate phosphoinositide hydrolysis and activate protein kinase C. The present study examined the role of group I mGluRs in nociceptive processing and capsaicin-induced central sensitization of primate spinothalamic tract (STT) cells in vivo. In 10 anesthetized male monkeys (Macaca fascicularis) extracellular recordings were made from 20 STT cells in the lumbar dorsal horn. Responses to brief (15 s) cutaneous stimuli of innocuous (BRUSH) and barely and substantially noxious (PRESS and PINCH, respectively) intensity were recorded before, during, and after the infusion of group I mGluR agonists and **antagonists** into the dorsal horn by microdialysis. Cumulative concentration-response relationships were obtained by applying different concentrations for at least 20 min each (at 5 microl/min). The actual concentrations reached in the tissue are 2-3 orders of magnitude lower than those in the microdialysis fibers (values in this paper refer to the latter). The group I **antagonists** were also applied at 10-25 min after capsaicin injection. S-DHPG, a group I agonist at both **mGluR1** and mGluR5, potentiated the responses to innocuous and noxious stimuli (BRUSH > PRESS > PINCH) at low concentrations (10-100 microM; n = 5) but had inhibitory effects at higher concentrations (1-10 mM; n = 5). The mGluR5 agonist CHPG (1 microM-100 mM; n = 5) did not potentiate but inhibited all responses (10-100 mM; n = 5). AIDA (1 microM-100 mM), a **mGluR1**-selective **antagonist**, dose-dependently depressed

the responses to PINCH and PRESS but not to BRUSH (n = 6). The group I (**mGluR1** > mGluR5) **antagonist** CPCCOEt (1 microM-100 mM) had similar effects (n = 6). Intradermal injections of capsaicin sensitized the STT cells to cutaneous mechanical stimuli. The enhancement of the responses by capsaicin resembled the potentiation by the group I mGluR agonist S-DHPG (BRUSH > PRESS > PINCH). CPCCOEt (1 mM) reversed the capsaicin-induced sensitization when given as posttreatment (n = 5). After washout of CPCCOEt, the sensitization resumed. Similarly, AIDA (1 mM; n = 7) reversed the capsaicin-induced sensitization and also blocked the potentiation by S-DHPG (n = 5). These data suggest that the **mGluR1** subtype is activated endogenously during brief high-intensity cutaneous stimuli (PRESS, PINCH) and is critically involved in capsaicin-induced central sensitization.

L19 ANSWER 4 OF 8 MEDLINE on STN

AB To investigate the role of Group I mGluRs in allodynia and hyperalgesia, we examined the behavioural responses of rats to noxious and non-noxious mechanical and thermal stimuli following intrathecal (i.t.) treatment (25 nmol) with the selective **mGluR1**/5 agonist, (RS)-dihydroxyphenylglycine ((RS)-DHPG). (RS)-DHPG administration produced a persistent decrease in response latency on a 48 degrees C hotplate, a reduction in the 50% response threshold to von Frey hairs, and an increase in responses to a tail pinch. These data suggest that activation of spinal **mGluR1**/5 receptors plays a role in the development of persistent allodynia and hyperalgesia associated with tissue or nerve injury.

L19 ANSWER 5 OF 8 MEDLINE on STN

AB To examine the specific roles of group I metabotropic glutamate receptors (mGluRs) in nociceptive processing, we examined the effects of intrathecal (i.t.) treatment with antibodies raised against the C-terminals of **mGluR1** and mGluR5 in various rat **pain** models. The effects of anti-**mGluR1** IgG and anti-mGluR5 IgG were assessed in a model of persistent **pain** induced by intrathecal administration of the **mGluR1**/5 agonist DHPG, as well as in models of heat **pain** (plantar test), chemical **pain** (formalin test) and neuropathic **pain**. DHPG-induced spontaneous nociceptive behaviours (SNB) were significantly attenuated by i.t. treatment with either anti-**mGluR1** IgG (30 microg) or anti-mGluR5 IgG (10 and 30 microg). Neither anti-**mGluR1** IgG (30 microg) nor anti-mGluR5 IgG (30 microg) significantly increased response latencies to noxious heat in the plantar test, compared with anti-rat IgG (control IgG). Moreover, neither antibody (30 microg) significantly reduced formalin **pain** scores as compared to control IgG. However, i.t. treatment with anti-**mGluR1** IgG (30 microg) or anti-mGluR5 IgG (30 microg) significantly reduced cold hypersensitivity exhibited 8 days after constriction injury of the sciatic nerve, supporting the contention that group I mGluRs play a role in the development of neuropathic **pain** . Because these antibodies were effective against neuropathic **pain**, and not acute heat or chemical noxious stimuli, these results suggest that mGluRs are involved in nociceptive processing in chronic **pain** states rather than signaling acute noxious stimuli, and that DHPG-induced **pain** may be mediated by similar mechanisms as neuropathic **pain**.

L19 ANSWER 6 OF 8 MEDLINE on STN

AB A combined study of behavioural and electrophysiological tests was carried out in order to assess the role of metabotropic glutamate receptors (mGluRs) in mediating sensory inputs to the spinal cord of the rat. In the behavioural study the responses of conscious animals, with or without carrageenan-induced inflammation, to noxious mechanical and thermal stimuli were observed both before and after the intrathecal administration of mGluR **antagonists** L(+)-2-amino-3-phosphonopropionic acid

(L-AP3) and (S)-4-carboxy-3-hydroxyphenylglycine (CHPG). It was found that the mGluR **antagonist** (S)-CHPG was capable of increasing both mechanical threshold and thermal latency in both groups of animals, and L-AP3 did so in those with inflammation induced in their hindpaw. Following this study, the responses of single lamina III-V dorsal horn neurons to an innocuous A beta fibre brush stimulus and a noxious C fibre (mustard oil) stimulus were extracellularly recorded and the effect of ionophoretically applied drugs was examined. Cyclothiazide (CTZ), a selective **antagonist** at **mGluR1**, markedly reduced the activity evoked by mustard oil, but not that elicited by brushing of the receptive field. Activity induced in dorsal horn neurons by ionophoresing various mGluR subgroup agonists was examined. CTZ successfully inhibited the activity evoked by group I mGluR agonist 3,5-dihydroxyphenylglycine (DHPG). In comparison to the neurons which responded to the ionophoresis of DHPG, less were activated by the selective mGluR5 agonist trans-azetidine dicarboxylic acid (t-ADA). Together these results indicate that group I mGlu receptors, in particular **mGluR1**, play a crucial role in mediating nociception, particularly following a sustained noxious input.

L19 ANSWER 7 OF 8 MEDLINE on STN

AB We examined the pharmacological profile of 1-aminoindan-1,5-dicarboxylic acid (AIDA), a rigid (carboxyphenyl)glycine derivative acting on metabotropic glutamate receptors (mGluRs). In cells transfected with mGluR1a, AIDA competitively **antagonized** the stimulatory responses of glutamate and (1S,3R)-1-aminocyclopentane-1,3-dicarboxylic acid [(1S,3R)-ACPD] on phosphoinositide hydrolysis (pA2 = 4.21). In cells transfected with mGluR5a, AIDA displayed a much weaker **antagonist** effect. In transfected cells expressing mGluR2, AIDA (< or = 1 mM) did not affect the inhibition of forskolin-stimulated adenylate cyclase activity induced by (1S,3R)-ACPD, but at large concentrations, it displayed a modest agonist activity. In rat hippocampal or striatal slices, AIDA (0.1-1 mM) reduced the effects of (1S,3R)-ACPD on phospholipase C but not on adenylate cyclase responses, whereas (+)-alpha-methyl-4-carboxyphenylglycine (0.3-1 mM) was an **antagonist** on both transduction systems. In addition, AIDA (0.3-1 mM) had no effect on mGluRs coupled to phospholipase D, whereas (+)-alpha-methyl-4-carboxy-phenylglycine (0.5-1 mM) acted as an agonist with low intrinsic activity. In rat cortical slices, AIDA **antagonized** the stimulatory (**mGluR1**-mediated) effect of (1S,3R)-ACPD on the depolarization-induced outflow of D-[3H]aspartate, disclosing an inhibitory effect ascribable to (1S,3R)-ACPD activating mGluR2 and/or mGluR4. Finally, mice treated with AIDA (0.1-10 nmol i.c.v.) had an increased **pain** threshold and difficulties in initiating a normal ambulatory behavior. Taken together, these data suggest that AIDA is a potent, selective and competitive **mGluR1** a **antagonist.**

L19 ANSWER 8 OF 8 MEDLINE on STN

AB The present study examined the role of mGluRs in nociceptive responses of male Long-Evans rats following a subcutaneous (s.c.) injection of 1% (30 microliters) or 2.5% (50 microliters) formalin to the plantar surface of the hindpaw. Intrathecal (i.t.) administration of the mGluR4/mGluR6-mGluR8 agonist, L(+)-2-amino-4-phosphonobutyric acid (L-AP4), the **mGluR1**/mGluR5 **antagonists.** (S)-4-carboxyphenylglycine ((S)-4CPG) or (S)-4-carboxy-3-hydroxyphenylglycine ((S)-4C3HPG), but not the non-selective **antagonist**, (+)-alpha-methyl-4-carboxyphenylglycine ((+)-MCPG), to the lumbar spinal cord slightly reduced second phase nociceptive responses. An i.t. injection of the **mGluR1**/mGluR5 agonist, (RS)-3,5-dihydroxyphenylglycine ((RS)-DHPG) or the mGluR2/mGluR3 agonist, (1S,3S)-1-aminocyclopentane-1,3-dicarboxylic acid ((1S,3S)-ACPD), but not (2S,1'R,2'R,3'R)-2-(2'3-dicarboxy-cyclopropyl)-glycine (DCG-IV),

dose-dependently enhanced formalin-induced nociception in the second phase. In addition, the facilitation of nociceptive responses induced by (1S,3S)-ACPD or (RS)-DHPG was reduced by prior i.t. administration of the mGluR **antagonists**, (+)-MCPG or (S)-4C3HPG, respectively, as well as by the N-Methyl-D-aspartate (NMDA) receptor **antagonist**, D(-)-2-amino-5-phosphonopentanoic acid (D-AP5). These results indicate that although mGluRs may play a minor role in formalin-induced nociception, mGluR agonist-related facilitation of formalin scores may reflect an interaction with the NMDA receptor.

=> s l15 and thalam?
37025 THALAM?
L20 24 L15 AND THALAM?

=> d 1-24 ti

L20 ANSWER 1 OF 24 MEDLINE on STN
TI Somatosensory corticothalamic projections: distinguishing drivers from modulators.

L20 ANSWER 2 OF 24 MEDLINE on STN
TI Metabotropic glutamate 2/3 receptors as drug targets.

L20 ANSWER 3 OF 24 MEDLINE on STN
TI Role of **thalamic** phospholipase C[beta]4 mediated by metabotropic glutamate receptor type 1 in inflammatory pain.

L20 ANSWER 4 OF 24 MEDLINE on STN
TI Group I metabotropic glutamate receptors in the monkey striatum: subsynaptic association with glutamatergic and dopaminergic afferents.

L20 ANSWER 5 OF 24 MEDLINE on STN
TI 2,4-Dicarboxy-pyrroles as selective non-competitive **mGluR1** antagonists: further characterization of 3,5-dimethyl pyrrole-2,4-dicarboxylic acid 2-propyl ester 4-(1,2,2-trimethyl-propyl) ester and structure-activity relationships.

L20 ANSWER 6 OF 24 MEDLINE on STN
TI Effect of phospholipase Cbeta4 lacking in **thalamic** neurons on electroencephalogram.

L20 ANSWER 7 OF 24 MEDLINE on STN
TI Induction mechanisms for L-LTP at **thalamic** input synapses to the lateral amygdala: requirement of mGluR5 activation.

L20 ANSWER 8 OF 24 MEDLINE on STN
TI Completing the corticofugal loop: a visual role for the corticogeniculate type 1 metabotropic glutamate receptor.

L20 ANSWER 9 OF 24 MEDLINE on STN
TI Up-regulation of metabotropic glutamate receptor 3 mRNA expression in the cerebral cortex of monoarthritic rats.

L20 ANSWER 10 OF 24 MEDLINE on STN
TI Expression of metabotropic glutamate receptors mRNA in the **thalamus** and brainstem of monoarthritic rats.

L20 ANSWER 11 OF 24 MEDLINE on STN
TI Human TREK2, a 2P domain mechano-sensitive K+ channel with multiple regulations by polyunsaturated fatty acids, lysophospholipids, and Gs, Gi, and Gq protein-coupled receptors.

Glutamate receptor antagonists for neuropathic pain

L20 ANSWER 12 OF 24 MEDLINE on STN
TI Differential distribution of metabotropic glutamate receptor subtype mRNAs in the **thalamus** of the rat.

L20 ANSWER 13 OF 24 MEDLINE on STN
TI Metabotropic glutamate receptor mRNA expression in the schizophrenic **thalamus.**

L20 ANSWER 14 OF 24 MEDLINE on STN
TI Differential expression of glutamate receptors by the dopaminergic neurons of the primate striatum.

L20 ANSWER 15 OF 24 MEDLINE on STN
TI Role of metabotropic glutamate receptor subtype **mGluR1** in brief nociception and central sensitization of primate STT cells.

L20 ANSWER 16 OF 24 MEDLINE on STN
TI A monoclonal antibody shows discrete cellular and subcellular localizations of **mGluR1** alpha metabotropic glutamate receptors.

L20 ANSWER 17 OF 24 MEDLINE on STN
TI Ultrastructural localization suggests that retinal and cortical inputs access different metabotropic glutamate receptors in the lateral geniculate nucleus.

L20 ANSWER 18 OF 24 MEDLINE on STN
TI The function of metabotropic excitatory amino acid receptors in synaptic transmission in the **thalamus**: studies with novel phenylglycine antagonists.

L20 ANSWER 19 OF 24 MEDLINE on STN
TI Metabotropic glutamate receptors are differentially regulated during development.

L20 ANSWER 20 OF 24 MEDLINE on STN
TI Changes in metabotropic glutamate receptor mRNA levels following global ischemia: increase of a putative presynaptic subtype (mGluR4) in highly vulnerable rat brain areas.

L20 ANSWER 21 OF 24 MEDLINE on STN
TI Differential localization of phosphoinositide-linked metabotropic glutamate receptor (**mGluR1**) and the inositol 1,4,5-trisphosphate receptor in rat brain.

L20 ANSWER 22 OF 24 MEDLINE on STN
TI Signal transduction, pharmacological properties, and expression patterns of two rat metabotropic glutamate receptors, mGluR3 and mGluR4.

L20 ANSWER 23 OF 24 MEDLINE on STN
TI Distribution of the mRNA for a metabotropic glutamate receptor (**mGluR1**) in the central nervous system: an in situ hybridization study in adult and developing rat.

L20 ANSWER 24 OF 24 MEDLINE on STN
TI Cellular localization of a metabotropic glutamate receptor in rat brain.

=> d 5 abs bib

L20 ANSWER 5 OF 24 MEDLINE on STN
AB Following the disclosure of 3,5-dimethyl pyrrole-2,4-dicarboxylic acid 2-propyl ester 4-(1,2,2-trimethyl-propyl) ester [3,5-dimethyl PPP] as a potent and selective **mGluR1** non-competitive antagonist, we

report here further in vivo characterization of this important tool and disclose the investigation of the C-5 position, which led to very potent compounds.

AN 2003271664 MEDLINE

DN PubMed ID: 12798316

TI 2,4-Dicarboxy-pyrroles as selective non-competitive **mGluR1** antagonists: further characterization of 3,5-dimethyl pyrrole-2,4-dicarboxylic acid 2-propyl ester 4-(1,2,2-trimethyl-propyl) ester and structure-activity relationships.

AU Micheli Fabrizio; Di Fabio Romano; Bordi Fabio; Cavallini Palmina; Cavanni Paolo; Donati Daniele; Faedo Stefania; Maffeis Micaela; Sabbatini Fabio Maria; Tarzia Giorgio; Tranquillini Maria Elvira

CS GlaxoSmithKline Medicine Research Centre, Via Fleming 4, 37135, Verona, Italy.. fabio@gsk.com

SO Bioorganic & medicinal chemistry letters, (2003 Jul 7) Vol. 13, No. 13, pp. 2113-8.
Journal code: 9107377. ISSN: 0960-894X.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200403

ED Entered STN: 20030612
Last Updated on STN: 20040302
Entered Medline: 20040301

=> d 18 abs bib

L20 ANSWER 18 OF 24 MEDLINE on STN

AB The phenylglycines 3-hydroxyphenylglycine, 4-carboxy-3-hydroxy-phenylglycine (4C3HPG), 4-carboxyphenylglycine (4CPG) and alpha-methyl-4-carboxyphenylglycine (MCPG) were evaluated as putative selective antagonists of metabotropic glutamate receptors on single neurones of the ventrobasal **thalamus** of rats, with a view to using these compounds as tools to elucidate synaptic mechanisms in this brain area. The S-isomers of the latter three compounds were found to reduce excitations evoked by iontophoretically applied 1S,3R-ACPD, but not those evoked by ionotropic excitatory amino receptor agonists. When the antagonists were tested against sensory synaptic responses of ventrobasal neurones, it was found that responses evoked by noxious thermal stimulation of the peripheral receptive field were reduced in parallel with responses to 1S,3R-ACPD. In contrast, responses of neurones evoked by non-noxious (air-jet) stimuli were not reduced by the phenylglycine antagonists and 4C3HPG was found to enhance such responses, possibly by a presynaptic action mediated via mGluR2 receptors. The reductions of nociceptive responses are discussed in the context of antagonism of **mGluR1** receptors, which are known to be numerous in the **thalamus** and located on post-synaptic dendrites. The involvement of such receptors in the nociceptive responses of **thalamic** neurones may be of considerable functional significance.

AN 95375680 MEDLINE

DN PubMed ID: 7647700

TI The function of metabotropic excitatory amino acid receptors in synaptic transmission in the **thalamus**: studies with novel phenylglycine antagonists.

AU Salt T E; Eaton S A

CS Department of Visual Science, Institute of Ophthalmology, London, U.K.

SO Neurochemistry international, (1994 May) Vol. 24, No. 5, pp. 451-8.
Journal code: 8006959. ISSN: 0197-0186.

CY ENGLAND: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)

LA English

Glutamate receptor antagonists for neuropathic pain

FS Priority Journals
EM 199509
ED Entered STN: 19951005
Last Updated on STN: 19951005
Entered Medline: 19950928

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.18	189.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-2.21

FILE 'STNGUIDE' ENTERED AT 09:00:06 ON 21 MAR 2006

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Mar 17, 2006 (20060317/UP).

=> logoff
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:n

=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):10603936
10603936 IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,
structure, or screen set), /A for an answer
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):neuropathic
NEUROPATHIC IS NOT A VALID SAVED NAME
Enter the name you wish to use for the saved query,
answer set, or L-number list. The name must:
1. Begin with a letter,
2. Have 1-12 characters,
3. Contain only letters (A-Z) and numbers (0-9),
4. End with /Q for a query (search profile,
structure, or screen set), /A for an answer
set, or /L for an L-number list.
5. Not already be in use as a saved name,
6. Not be END, SAV, SAVE, SAVED
7. Not have the form of an L-number (Lnnn).
ENTER NAME OR (END):neuropath/a
'NEUROPATH/A' IS NOT ALLOWED WITH ALL
The saved name of an L# list must end with '/L'.

=> lneuroapth/l
LNEUROAPTH IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.

Glutamate receptor antagonists for neuropathic pain

For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> exit
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.36	190.16

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-2.21

STN INTERNATIONAL LOGOFF AT 09:03:59 ON 21 MAR 2006